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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/902,563	07/12/2001	Gary Levy	9579-37	4438

7590 06/17/2003

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/17/2003

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/902,563	LEVY, GARY	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *15 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 5/15/03 (Paper No. 6), is acknowledged.

2. Claims 1-4 are pending and under consideration in the instant application.

3. In view of the amendment filed on 5/15/03 (Paper No. 6), only the following rejections remained.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for a method of preventing or treating intestinal transplants and xenogeneic hyperacute liver failure comprising administering an antibody to SEQ ID NO:2 or SEQ ID NO:18 to an animal, does not reasonably provide enablement for a method of preventing or treating any graft rejection comprising administering any inhibitor of Fgl2 to an animal, wherein the inhibitor is any antibody that binds to Fgl2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims for the same reasons set forth in the previous Office Action, paper No. 4, mailed 12/17/02.

Applicant's arguments, filed 5/15/03 (Paper No. 6), have been fully considered, but have not been found convincing.

Applicant asserts that Graft rejection of all tissues and organs work by common phenomena-the recipient mounts an immune and inflammatory response to the foreign tissue or organ. Applicant asserts that he has determined that Fgl2 is an immune coagulant that is involved in transplant rejection. Applicant argues that he should not be limited to a particular type of transplant as the involvement of Fgl2 would be the same in respect of the rejection of any transplant. Applicant further argues that he provided three distinct examples of how inhibting Fgl2 can be used to prolong graft survival. For example, applicant has shown the antibodies to Fgl2 are useful in preventing rejection of a small intestinal allograft, and the prevention of a liver xenograft. Applicant further argues that the other examples (4&5) show that antibodies to Fgl2 can prevent fetal loss, wherein the fetus is a well accepted type of transplant as the maternal and fetal tissues are not identical. Applicant provides additional data to show that antibodies to Fgl2 can prolong the survival of a heart transplant as submitted Declaration under 37 CFR 1.132 executed by inventor Gary Levy. Applicant concluded that by enabling the invention using antibodies to Fgl2 would by sufficient to enable one of skill in the art to use any other inhibitor of Fgl2 such as antisense molecules in order to practice the invention. Applicant further draws

Examiner attention to the following paper to demonstrate that one skilled in the art could readily isolate Fgl2 inhibitors that may be used in the invention.

Ning Q et al., J Immunol. 160(7):3487-93, 1998 and
Marazzi S et al., J Immunol. 161(1):138-47, 1998.

Contrary to the applicant assertions the specification falls to provide sufficient guidance regarding preventing and treating any graft rejection. For example, Krenger and Ferrara (immunol. Res. 15:50-73, 1996) describe the development of acute Graft-versus-Host disease as a three-step process. Specially, donor T cell activation during the second step of Graft-versus-Host Disease pathophysiology is characterized by proliferation of type 1 T cells and secretion of IL-2 and IFN-γ. Moreover, Krenger and Ferrara teach that distinct immunological patterns observed in two murine models of a cute and chronic graft-versus-host disease are associated with differential activation of Type I and type 2 T cell subsets after allogeneic BMT (see page 61, 2nd col., lines 29-33). Further, Krenger and Ferrara teach that a classical lethal acute GVHD is linked to the preferential activation of donor T cells secreting Il-2 and IFN-γ which the less severe chronic form of GVHD is characterized a type 2 cytokine response where IL-4 and IL-10 are preferentially produced after BMT (see page 61, 2nd col., lines 38-43 and page 62, lines 1-10). Thus, the specification does not provide sufficient enablement for the preventing and treat any graft rejection. Furthermore, Toogood et al (Transplantion 62:851-855, 1996) teaches that the mechanisms of rejection in small bowel and other solid organ grafts are likely to be different (see abstract in particular). Toogood et al concluded that there are significant immunological differences between the gut wall compartment of a small bowel transplant and other vascularized allografts (sse page 855, 1st col., lines 13-16 in particular). Therefore, it is not clear that the skilled artisan could predict the efficacy of the anti-Fgl2 mAb exemplified in the specification to treat any graft rejection.

While Levy Declaration filed on 5/15/03 under 37 CRF 1.132 provides the use of Fgl2 antibodies to increase the survival of the cardiac allograft, Applicant still not enabled for all types of graft rejection because not all tissues and organs graft rejects work by a common mechanism.

Regarding Fgl2 inhibitor, Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. The claims as written encompass a broad genus of Fgl2 inhibitors with an unlimited number of possibilities with regard to the candidate inhibitor. Further, the enablement issues of making those inhibitors still remain because the specification does not teach and provide sufficient guidance as to which Fgl2 inhibitor would have the function of treating and prevention grafts. Therefore, absent the ability to predict which of these Fgl2 inhibitors would function as claimed, and given the lack of data on specific inhibitor beside the antibody to Fgl2, for one of skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

While both Ning et al and Marazzi et al provide Fgl2 antagonist, neither of those antagonist are show to prevent and treat graft rejections.

Consequently, without additional guidance in the specification, and the dearth of information in the art, for one of skill in the art to practice the invention as claimed, would require experimentation that is excessive and undue. The amount of guidance or direction needed to enable an invention is inversely related to the mount of knowledge in the state of the art as well as the predictability in the art (In re Fisher, 427 F.2d 833, 839, 166 USPQ 18,24 (CCPA 1970)).

5. Claims 1-4 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention claims for the same reasons set forth in the previous Office Action, paper No. 4, mailed 12/17/02.

Applicant's arguments, filed 5/15/03 (Paper No. 6), have been fully considered, but have not been found convincing.

Applicant argues that he is not attempting to claim Fgl2 per se, but rather to the use of Fgl2 inhibitors to prevent or treat graft rejection. Applicant has concluded "a single embodiment is representative of the genus". Applicant argues that the claims under examination are directed to a single embodiment (e.g. treatment of graft rejection by inhibiting Fgl2). Applicant argues that it is not necessary to include a description of a representative number of species. Applicant argues that the specification provides ample information on how Fgl2 inhibitors such as antibodies and antisense molecules can be prepared.

However, the Examiner notes that the claimed invention which is drawn to a genus may be adequately described if there is a (1) sufficient description of a representative number of species, or (2) by disclosure of relevant, identifying characteristics sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. To satisfy the disclosure of a "representative number of species" will depend on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. "Relevant, identifying characteristics" include structure or other physical and /or chemical properties, functional characteristics coupled with a known or disclosed correlation between function and structure, or a combination of such identifying characteristics sufficient to show the applicant was in possession of the claimed genus. (see Revised Guidelines for the Examination of Patent Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001).

In the instant case, however, there is no described or art-recognized correlation or relationship between the structure of the invention, the antibodies to SEQ ID NO:2 or 18 and it's inhibition of immune coagulation , the feature deemed essential to the instant invention. Therefore, one of

skill in the art would not envisage, based on the instant disclosure, the claimed genus of Fgl2 inhibitors.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-4 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 22-23 and 34 of copending Application No. 10/096,255. Although the conflicting claims are not identical, they are not patentably distinct from each other because the specification of application No. 10/096,255 indicates that the inhibitor of Fgl2 includes the monoclonal antibody that binds to SEQ ID NO: 2 and SEQ ID NO: 18 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant indicates that a terminal Disclaimer will be filed or the overlapping claims of the copending application will be removed once an indication that the current claims are allowable.

8. No claim allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

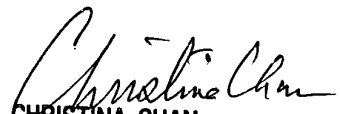
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
June 16, 2003



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